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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,711	04/20/2001	Darwin J. Prockop	57616-5017US1	6580

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EXAMINER

KELLY, ROBERT M

ART UNIT	PAPER NUMBER
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1633

DATE MAILED: 07/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/839,711	Applicant(s) PROCKOP ET AL.	
	Examiner Robert M. Kelly	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicant's response of 6/13/06 is entered.

Claims 17, 21, 25, 29-32 have been amended.

Claims 17-32 are presently pending and considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

In light of Applicant's amendments, the rejections of Claims 17-32 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, in the official Action of 2/10/06, are withdrawn.

Claims 17-32 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons necessitated by the amendments.

Claims 17, 21, 25, and 29-32 each recite "said isolated bone marrow stromal cells are isolated away from non-adherent cells in bone marrow". It is unclear what such non-adherent cells are non-adherent to.

Claims 18-20, 22-24, and 26-28 are rejected for depending from a rejected base claim and not overcoming the lack of clarity in such base claim.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of Applicant's amendments, the rejections of Claims 17-32 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, in the Official Action of 2/10/06, are withdrawn

Claims 17-32 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons necessitated by amendment. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 17, 21, 25, and 29-32, and their dependent claims, each encompass bone marrow stromal cells that are isolated from non-adherent cells of bone marrow.

Applicant argues that the definition of bone marrow stromal cells, stating that these cells "can be isolated from bone marrow by their ability to adhere to plastic dishes", and that Applicant's example I, demonstrating isolation by discarding the non-adherent cells of a culture, provide ample support for Applicant's claimed limitation (Applicant's argument of 6/13/06, p. 6, paragraph 3). Moreover, the Examiner has failed to find any better support for this limitation in the specification.

However, Applicant's definition does not state that these cells should be isolated, and Applicant's example is implicit, and therefore would be limited to same cells and animals and

Art Unit: 1633

culturing in the example. Moreover, the term “non-adherent cells” is broad, and simply is not supported for its breadth by this limitation.

Therefore, the Artisan would understand Applicant to have been in possession of the invention as presently claimed due to this limitation.

Hence, these claims comprise new matter.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-32 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons necessitated by amendment. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant’s claims encompass the limitation of culturing bone marrow stromal cells “for one hour to a year”.

Applicant argues that the specification provides support for this limitation, and the Examiner has found no better support, by the statement “Isolated stromal cells can be cultured from 1 hour to up to over a year.” (Applicant’s argument of 6/13/06, p. 6, paragraph 3; SPECIFICATION, p. 9, paragraph 1).

Art Unit: 1633

However, such statements are not equivalent. It is clear from the specification that such statement encompasses much more than “up to one year”, but instead encompasses anything over a year. Therefore, the Artisan would not understand Applicant to have been in possession of the claimed invention at the time of filing.

Hence, Applicant’s claims encompass new matter.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-32 are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons necessitated by the amendments. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant’s claims encompass methods for any mammal wherein the DNA from the isolated bone marrow stromal cells are not detected in the bone marrow in the mammal treated.

Applicant’s support is implicit, relying on an implicit example wherein rats are tested under a specific testing procedure to determine that no donor DNA is detected in bone marrow (Applicant’s response of 6/13/06, p. 6, paragraph 3). However, such implicit example is limited to that procedure used, with the same materials. Such is because the whole of the specification teaches that such donor cells, and therefore, necessarily, their DNA are localized to the bone

Art Unit: 1633

marrow. Further, the Art supports the same conclusion, e.g., Ankelsaria (1987) Proc. Natl. Acad. Sci, USA., 84: 7681-85, whole of article. Hence, the DNA may be detected, based on method. Moreover, there is no explicit disclosure found in the specification to support the broader genera claimed.

Hence, Applicant's claims are rejected for comprising new matter.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-32 remain rejected under 35 U.S.C. 102(b) as being anticipated by Remes, et al. (1996) Ann. Med., 28: 79-81, for reasons of record.

Applicant's claims are now limited to the isolated bone marrow stromal cells being isolated from non-adherent cells in bone marrow, and that subsequently treated patients do not contain detectable levels of donor DNA in their bone marrow.

With regard to non-adherent cells in the bone marrow, it is axiomatic that the cells that were isolated from the patient did not adhere to the cells of the bone marrow that were left behind in the patient, and therefore, such limitation is met inherently.

With regard to the absence of detection, if the method was performed, the limitation must have been met.

Response to Argument – anticipation, Remes

Applicant's argument of 6/13/06 has been fully considered but is not found persuasive.

Applicant argues that the claims recite *in vitro* culturing for 1 hour to a year, and therefore, the claims are no longer anticipated by Remes (p. 8, paragraph 6).

Such is not persuasive. Applicant's claims also encompass administration of the cells immediately upon isolation, and such is in alternative form. Hence, the claims are still anticipated.

Applicant argues that Remes does not teach isolated bone marrow stromal cells (p. 8, last paragraph).

Such is not persuasive. These cells are isolated from a patient, and therefore, they are isolated.

Applicant argues that Remes does not teach or suggest bone marrow stromal cells, and is limited to hematopoietic stem cells (pp. 8-9, paragraph bridging).

Such is not persuasive. As has been discussed in the prior Official Action, these bone marrow transplants inherently contain bone marrow stromal cells.

Applicant argues that Remes, in discussing other stem cells, distinguishes the methods presently claimed (Id.).

Such is not persuasive. Remes teaches that the bone marrow may be used, and hence, it anticipates the claims.

Claim Rejections – 35 USC § 103 – Anklesaria/Palsson

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 17-32 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Ankelsaria and U.S. Patent No. 5,635,386 to Palsson, et al., as further evidenced by Shpall, et al. (1997) Annu. Rev. Med., 48: 241-51; Remes, et al. (1996) Annals Medicine, 28 : 79-81, and Piersma, et al. (1983) Brit. J. Haematology, 54: 285-90, for reasons of record.

It is noted that Applicant's claims now require the DNA not be detected, and it is noted that Ankelsaria never detected the donor DNA in the marrow. Hence, the claims are still obvious. Moreover, with regard to the culturing, it would be obvious to culture the cells for a period of between 1 hour and 1 year, to expand them to the point required for the transplantation, as taught in the references and discussed previously.

Response to Argument – Ankelsaria/Palsson

Applicant's response of 6/13/06 has been fully considered but is not found persuasive.

Applicant argues that Wertz is not supplied and not considered (p. 9, last paragraph).

Such is persuasive. The Examiner decided not to provide Wertz, but, due to typographical error, missed removing the Art from the rejection.

Applicant argues that Ankelsaria teaches that the cells engraft in the bone marrow, and therefore, the limitation to not detecting DNA is not taught or suggested (p. 10, paragraph 1).

Art Unit: 1633

Such is not persuasive. Ankelsaria never taught that it is required to detect the DNA. Second, Ankelaria never detected donor DNA, but instead detected the cells. Third Applicant's argument is that they have an invention which they themselves are not teaching the specification: the use of stromal cells to culture, *in vivo*, hematopoietic stem cells, to allow for reconstitution of the hematopoietic system (SPECIFICATION in general). Moreover, Applicant's own specification teaches that such occurs in the bone marrow, and that Applicant's only support for such non-detection of DNA is limited to demonstrating that the donor cells are not part of the hematopoietic stem cells, not the bone marrow stromal cells (EXAMPLES). Hence, its clear Applicant's limitation is not what they are arguing, but instead that no one detects the DNA, not that the cells are not there, containing their DNA.

Applicant argues that Palsson teaches culturing cells in vitro, and does not teach or suggest the therapeutic methods using hematopoietic stem cells (p. 10, paragraph 3).

Such is not persuasive. Palsson is not required to teach or suggest therapeutic methods according to Applicant's argument, as this is an obviousness rejection, not a rejection for anticipation.

Applicant argues, individually, that each of Shpall, Remes and Piersma, do not teach or suggest various limitations, and therefore, they do not apply to the rejection (p. 11).

Such is not persuasive. Applicant fails to appreciate that these references are provided together, and are not even part of the rejection, but demonstrating further evidence that the Artisan would have found the methods obvious. The Examiner maintains that, given this evidence, the Artisan would have found the methods obvious, for reasons of record.

Note to Applicant

Applicant appears to believe that their disclosure of essentially the same thing as Ankelsaria enables their invention at the time of invention, with a breadth of many species and cell types, but that Ankelsaria's invention is not obvious for any more than what is shown in the reference itself, at the time of Applicant's invention. On the hand, the Examiner believes that the art sufficiently demonstrates those aspects claimed by Applicant are enabled by the Ankelsaria reference. Further to this point, if two references disclose the same thing at the same time, they necessarily enable, and therefore provide a reasonable expectation of success for the same subject matter. The Examiner has demonstrated that bone marrow transplants were known in the art, that the stromal cells were the reasons for such transplants, and that other references recognize the utilization of stromal cells in, *inter alia*, humans, even to the point of suggesting a different source for equivalent cells (i.e., peripheral blood). Such suggestion and application of a different source would not be made if the Art did not have the field pretty well characterized. Moreover, with regard to the differences in Ankelsaria, those differences between Ankelsaria and Applicant's disclosure encompass such structure that would not be detrimental to a reasonable expectation of success (i.e., the transformation yielded cells with equivalent function). Moreover, the whole of the Palsson reference takes for granted that these cells are used in such methods of transplantation. Hence, the only conclusion that can be reasonably made by the Artisan is that Applicant's claimed methods are obvious.

Conclusion

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1633

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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